Totally implantable central venous catheters for chemotherapy: experience with 793 patients

Cateteres venosos centrais totalmente implantáveis para quimioterapia: experiência com 793 pacientes

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A B S T R A C T

Objective: To retrospectively study the results obtained with the implementation of totally implantable catheters in patients undergoing chemotherapy. **Methods**: 815 totally implantable catheters placed in 793 patients undergoing chemotherapy regimen, preferably using the right cephalic vein. We evaluated early and late complications. **Results**: The retrospective analysis showed an average duration of 339 days of the catheters. In 733 (90%) catheters there was no observe complication. Among early complications we observed one pneumothorax, one bad positioning of the catheter, one arterial puncture, one bleeding, one hemothorax and hemomediastinum and six hematomas in the implantation site. As for late complications, there were 35 catheter-related infections ten, infections in the surgical site, six obstructions and 20 thromboses. We removed 236 catheters, 35 due to complications and 201 by the end of treatment. **Conclusion**: totally implantable catheters for chemotherapy are a safe means for the administration of substances, in view of the low number of complications observed in this study.

Key words: Drug therapy. Catheters. Catheters, indwellin. Central venous catheters. Infection.

INTRODUCTION

Totally implantable long-term central venous catheters (CVC) are commonly used in cancer patients for chemotherapy, parenteral nutrition, blood collection for tests and blood transfusion. Despite its benefits, the CVC is associated with significant morbidity and mortality. Those for chemotherapy are made of silicone. They have their distal end positioned at the junction of the superior vena cava with the right atrium, and the proximal, along its subcutaneous implantation site [1].

The totally implantable CVC are an excellent means of accessing the venous system, in addition to being effective and associated with a dwindling number of complications, especially when compared to other central venous catheters [2,3]. They need fewer manipulations, injections of heparin solution and dressings, and favorable aesthetic appearance due to being subcutaneous, not restricting patients' activities [4].

Although these catheters have become common in recent years, few studies have been done in Brazil, especially prospective ones, with a significant number of cases and long term follow-up.

In the present study we retrospectively evaluated the results obtained with the implementation of 815 totally implantable catheters in 793 patients undergoing chemotherapy in two large hospitals.

METHODS

We conducted a retrospective study with 793 patients suffering from malignant tumors, submitted to insertion of 815 totally implantable catheters for chemotherapy from March 2005 to September 2009,. The research took place in the San Marcos and Prontomed Hospitals, in the city of Teresina, Piauí State, Brazil.

The study was approved by the Research Ethics Committee of the Federal University of Piauí – UFPI (CAAE: 0400.0.045.000-11).

All catheters were placed by the same surgeon, using the open technique. All procedures were performed in the operating room, with the assistance of the anesthesiologist.

The operations were performed under local anesthesia, with sedation with intravenous propofol. All patients received antibiotic prophylaxis with 1g cefazolin at induction of anesthesia.

Patients received a leaflet containing information about the signs and symptoms of complications and the

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need to inform the surgeon about any abnormality resulting from the procedure.

The first option was to access the right cephalic vein. When this displayed an inadequate diameter for placement of the catheter, we proceeded to dissection of the external jugular vein. The puncture was performed when we could not access by dissection. The puncture was first attempted in the subclavian vein and, as a second option, the internal jugular vein. Table 1 shows the access routes and techniques employed. No catheter was introduced when there was the presence of fever of unknown origin, any systemic infectious condition (bacteremia or septicemia) or signs of skin infection near the site for insertion.

We used intraoperative fluoroscopy to position the catheter tip in the superior vena cava, near the entrance to the right atrium. We did not perform routine venography or Doppler ultrasound of the great vessels, but in individuals who had symptoms of deep vein thrombosis.

Patients who had catheters implanted in the saphenous vein showed great vessels thrombosis or non-progression of the catheter due to mediastinal lymphadenopathy or infection in the upper cervical or subclavian regions.

Complications were classified into immediate / early (intraoperative and postoperative before catheter use) and late (those occurring after the use of the catheter).

RESULTS

Patients' age ranged from 12 to 85 years, with an average of 50.8. Six hundred patients were female (75.7%) and 193 male (24.3%).

The main clinical indications for implantation of catheters were chemotherapy for treatment of solid tumors (87.5%) and hematologic diseases (12.5%). In 40.7% of patients, the tumor was located in the breast (Table 2). The procedure ranged from eight to 110 minutes, with an average of 17 minutes.

Of the 815 catheters, 82 (10%) had some type of complication. We removed 236 catheters, of which 201 (85%) were by elective indication due to the end of treatment and 35 (15%) resulted from complications that could not be controlled with clinical measures.

Among the early complications observed, there were six hematomas in the insertion site, five of which treated successfully by clinical measures and one, caused by puncture of the right carotid artery, treated conservatively; one small right pneumothorax which was also treated conservatively; one hemothorax and hemomediastinum resulting from puncture and insertion of the venous dilator in the left subclavian artery, the chest being drained; one bleeding, for which thromboprophylaxis was suspended and a pressure dressing applied for 48 hours; one case of bad positioning of the catheter, which was resolved by its replacement.

The other complications occurred at a later stage and involved 71 of the 815 catheters (8.7%). In four patients, more than one catheter complication was observed during follow-up: one patient had infection and venous thrombosis; one had infection and occlusion; one, infection and hematoma; and another, venous thrombosis and hematoma.

Infectious complications occurred in 35 patients (4.3%). *Pseudomonas sp*, *Klebsiella pneumoniae*, *Salmonella sp* and *E. coli* were the major etiological agents of catheter infections found in cultures and treated with proper antibiotics longer period of time, ranging from 14 to 21 days; the antibiogram showed sensitivity to ciprofloxacin, imipenem and meropenem. The catheter had to be removed in 16 cases due to prolonged fever or worsening of the patient's clinical status. In 19 cases there was an improvement in the clinical picture, with preservation of the catheter (preservation rate of 54.3%). Wound infection occurred in ten patients, all treated with intravenous antibiotics, and in six cases there was catheter removal.

Non-infectious complications occurred in 26 cases. In six cases, there was obstruction of the catheter. In 20

Table 1 - Access routes used for the implantation of a central venous catheter.

Vein accessed	Dissection	Puncture	n (%)
Right Cephalic Vein	515	0	63.2%
Left cephalic vein	126	0	15.5%
Right External Jugular Vein	66	0	8.1%
Left External Jugular Vein	19	0	2.3%
Right Subclavian Vein	0	50	6.1%
Left subclavian vein	0	10	1.2%
Right Internal Jugular Vein	0	14	1.7%
Left Internal Jugular Vein	0	08	1.0%
Right Saphenous Vein	04	0	0.5%
Left Saphenous Vein	01	0	0.1%
Right Femoral Vein	02	0	0.2%
Total	733 (90%)	82 (10%)	100%

Table 2 - Location of tumors with indication of central venous catheter.

Organ	N (%)
Breast	323 (40.7%)
Digestive Tract	130 (16.4%)
Ovary, uterus, prostate, testis, penis and vulva	118 (14.9%)
Lymphoma, leukemia	71 (8.9%)
Lung	53 (6.7%)
Soft tissue and skin	15 (1.9%)
Urologic (kidney, bladder and urethra)	6 (0.75%)
Other	77 (9.7%)
Total	793 (100%)

cases there was deep vein thrombosis associated with the catheter. In cases of obstruction, we trying to maintain the patency of the catheters, but in three cases patency was impossible and the catheters had to be removed, being replaced by another.

There were twenty cases of deep vein thrombosis: the majority affected the subclavian vein, followed by the internal jugular vein and there was only one case of superior vena cava thrombosis. By implementing the systemic anticoagulation with low molecular weight heparin and warfarin, it was possible to preserve ten of the 20 catheters (preservation rate of 50%). The catheters were removed in ten cases of deep vein thrombosis, which were associated with non-functioning catheters. None of these cases developed pulmonary thromboembolism. There was only one case of superior vena cava syndrome.

DISCUSSION

With the advent of chemotherapy, the search for safe and long lasting vascular accesses increased. Nowadays, the totally implantable central venous catheters are an excellent means of access to the bloodstream and are considered effective and associated with reduced incidence of complications. Kurul *et al*. [5] reported a significant reduction in the rates of complications as the team gained experience with central venous accesses [2,3,5]. A previously controversial condition, the cost-effectiveness of implantable devices becomes evident within six months, related to lower rate of complications and need for maintenance care [6,7].

The preferred access route for the implementation of the majority of long-term catheters is the dissection of the right cephalic vein, successfully used in 63.2% of our cases. This vein is a safe route because it is a superficial one, its dissection requires minimal tissue handling and, enabling faster and effective control of possible complications.

For some the preferred route is the subclavian vein [8], which is more associated with complications such as pneumothorax, hemothorax, arterial injury or compression of the catheter between the first rib and the clavicle. The surgical team is critical to the success of the procedure. The surgeon should be used to deal with different access routes, in order to provide the safest one, as well as be prepared for possible changes in the intraoperative conduct.

Early complications related to the procedure were properly diagnosed and treated. Such complications accounted for 1.3% of cases, hematoma at the insertion site being the most frequent, and were treated with surgical drainage. In this study there was no case of embolism by catheter fracture. Embolisms occur when there is a rupture of the catheter and a large fragment migrates to the vessel directly to the lung or heart, or when there is air in the system, infusion systems disconnections or empty solutions bottles, thereby characterizing gas embolisms, which are rare events [9]. Due to the improvement of equipment and insertion techniques, the complication rates are getting smaller. However, some recent studies show significant complication rates, with up to 2% incidence of pneumothorax, 14% of cardiac arrhythmia, 3% of arterial puncture, 3% of guide-wire bending and 3% of kinking of the introductory sheath [8,10,11]. In this study, the incidence of pneumothorax, arterial puncture, hemothorax and hemomediastinum and bad positioning was 0.12%, much lower than that shown in the literature; in addition, there was no case of cardiac arrhythmia.

Despite care, infection remains the main late complication, catheter-related bacteremia being the most frequent. The infection rate can reach 31%[12]. In this study, it was observed that catheter infections occurred in 4.3% of patients. Infection arise from the contamination by micro-organisms of the site of infusion or of the catheter from skin colonization, contaminated material, malfunction of the air inlet filter and from the catheter connections [9]. This condition should be suspected whenever the patient has fever and wound erythema. The proper use of asepsis techniques during catheter manipulation reduces its occurrence [9,13]. In our study, antibiotic prophylaxis was used in all procedures.

Non-infectious late complications can be divided in catheter obstructions and deep vein thrombosis. The incidence of these two is far from negligible. In the literature, the rates vary between 7% and 50% [14-17]. In our study there were 26 of these complications (3.2%). Deep vein thrombosis (DVT) in the veins of the upper compartment of the body is usually secondary to central venous catheters and cancer-related hypercoagulable state [18]. Regarding the catheter, there is: chemical structure, diameter, number of lumens, position the catheter tip, insertion side, implantation technique, prior use of central venous access and catheter-related infections. Patients' characteristics include: platelet count, presence and type of malignancy, chemotherapy protocol and hypercoagulable states [19]. The implantation of central venous access causes the endothelium to lose its integrity and leads to activation of procoagulant factors and platelets, thus forming thrombus [20]. The use of anticoagulants after placement of a totally implantable catheter for chemotherapy aiming to reduce thrombosis is controversial in the literature, with studies showing decreased thromboembolic events [20-23] and other not [24-26]. In this sample, there were 20 cases of deep vein thrombosis (2.4%), but removal of the catheter was necessary in ten patients (50%), due to their malfunctioning.

Deep vein thrombosis associated with central venous catheter is usually asymptomatic or presents with nonspecific symptoms [18,19]. Symptomatic patients commonly report discomfort in the shoulder or neck, and exhibit erythema, distal paraesthesia, congestion of the subcutaneous collateral veins and edema in the ipsilateral upper limb, the degree of venous obstruction being related to the signs and symptoms. In cases of obstruction of the superior vena cava, there is facial swelling, headache, visual changes, dizziness and breathlessness [18], simulating a superior vena cava syndrome.

Obstructions are defined when there is an impossibility or difficulty of infusing substances or drawing blood, being classified as total or partial. As regards to the source of obstruction, they can be mechanical, when compression or bending occurs; thrombotic, through the formation of fibrin internally or external to the catheter due to vascular lesions or hypercoagulable states; and non-thrombotic, due to precipitation of substances infused through the catheter [9,18,26]. In this article there were only six cases of obstruction, and in three the catheter was removed and replaced in the same procedure.

Totally implantable catheters for chemotherapy are a safe means for the administration of substances, in view of the low number of complications observed in this study. An experienced surgeon, ahead of the team, with a good technique for catheter implantation and strict asepsis, and monitoring of patients throughout the treatment, reduces early complications and prevents late ones.

R E S U M O

Objetivo: *estudar retrospectivamente os resultados obtidos com a implantação de cateteres totalmente implantáveis em pacientes submetidos à quimioterapia.* ***Métodos:*** *foram colocados 815 cateteres totalmente implantáveis em 793 pacientes submetidos ao regime de quimioterapia preferencialmente utilizando-se a veia cefálica direita. Foram avaliadas as complicações precoces e tardias.* ***Resultados:*** *a análise retrospectiva mostrou duração média dos cateteres de 339 dias. Em 733 (90%) cateteres não se observou nenhuma complicação. Entre as complicações precoces observamos um pneumotórax, um mau posicionamento de cateter, uma punção arterial, um sangramento, um hemotórax e hemomediastino e seis hematomas na loja de implantação. Entre as complicações tardias, ocorreram 35 infecções relacionadas ao cateter, dez infecções no sítio cirúrgico, seis obstruções e 20 tromboses. Foram retirados 236 cateteres, 35 devido às complicações e 201 por final de tratamento.* ***Conclusão:*** *os cateteres totalmente implantáveis para quimioterapia são meios seguros para a administração de substâncias, em vista do baixo número de complicações observadas neste estudo.*

Descritores: *Quimioterapia. Cateteres. Cateteres de demora. Cateteres venosos centrais. Infecção.*

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